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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,772	07/25/2003	Kazutomo Inoue	0020-5157P	1689

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EXAMINER

SGAGIAS, MAGDALENE K

ART UNIT	PAPER NUMBER
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1632

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	01/22/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary

Application No.

10/626,772

Applicant(s)

INOUE ET AL.

Examiner

Magdalene K. Sgagias

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 14 is/are pending in the application.
- 4a) Of the above claim(s) 7, 8, 11 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 9 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments filed 10/19/06 have been fully considered but they are not persuasive. The amendments have been entered. Claims 1-11 and 14 are pending. Claims 7-8, 11 and 14 are withdrawn to a non-elected invention. Claims 12-13 are cancelled. Claims 1-6 and 9-10 are under consideration.

Claim Objections

Claims 2 and 9-10 objection to minor informalities is withdrawn.

Claim Rejections - 35 USC § 112

Claims 1-6, 9-10, rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 4, rejection under 35 USC § 112, second paragraph, for insufficient antecedent basis is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 9-10 rejection under 35 U.S.C. & 102(a) as being anticipated by **Lumelsky et al**, (Science, 292: 1389-1394, 2001) is maintained for reasons discussed in the office action mailed 5/19/06.

Applicants argue that Lumelsky et al, uses no LIF in the ES cell media for EB formation, in contrast, the present method uses cell media containing LIF. These arguments are not persuasive. Applicants also argue Lumelsky et al, divide the selection and expansion stage into two stages (stages 3 and 4), in contrast, the present invention performs this in one step, step 3 and the preferred media comprises nicotinamide, fibronectin, and N2 supplements. These arguments are not persuasive.

Lumelsky teaches the expansion of ES cell in the presence of LIF for 2-3 days (see p 1390 figure 1) and the generation of EBs in the presence of bFGF (see p 1388, 2nd column, last three sentences). Lumelsky also teaches the cells were expanded in the presence of a mitogen, bFGF, in the N2 serum-free medium, followed by mitogen withdrawal to promote cessation of cell division and differentiation found that including in the culture media a B27 supplement and nicotinamide improved the yield of pancreatic endocrine cells, wherein the outcome is the production of many aggregate cells expressing insulin (p1388, 2nd column, bridge 3rd column).

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The as-filed specification does not disclose any differential properties of any of the insulin producing cells isolated by permutating the order of steps. See MPEP 2144.04 or MPEP 2111.01:

MPEP 2144.04

C. Changes in Sequence of Adding Ingredients

Ex parte Rubin , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

MPEP 2111.01:

Altiris Inc. v. Symantec Corp., 318 F.3d 1363, 1371, 65 USPQ2d 1865, 1869-70 (Fed. Cir. 2003) (Although the specification discussed only a single embodiment, the court held that it was improper to read a specific order of steps into method claims where, as a matter of logic or grammar, the language of the method claims did not impose a specific order on the performance of the method steps, and the specification did not directly or implicitly require a particular order).

Applicants argue, the ultrastructure and function of the differentiated insulin-producing cells of the presently claimed methods are different compared to Lumelsky et al. That is according to instantly claimed invention, insulin-producing cells differentiated from mES cells had an ultrastructure similar to beta cells. Applicants also argue as disclosed in the examples of the presently claimed invention, these cells were grafted in rats in which STZ was used to induce diabetes and blood glucose levels were restored in these rats. Applicants further argue the differences in the ultrastructure and function between the presently claimed invention and that of Lumelsky et al, are highlighted further by Rajagopal et al, in the enclosed Exhibit B, for the Examiner's convenience. These arguments are not persuasive.

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Lumelsky et al did not perform electron microscopy of the differentiate insulin producing cells nor did they perform grafting of these cells in rats in which STZ was used to induce diabetes and test if blood glucose levels were restored in these rats. Moreover, the claims as written do not require these tests. As such, the insulin producing cells of the instant invention and Lumelsky inherently carry these characteristics.

“[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency’ under 35 U.S.C. 102, on *prima facie* obviousness’ under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted].” The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Claims 1-6 rejection under 35 U.S.C. & 102(e) as being anticipated by Thomson et al, (US 6,602,711) is withdrawn.

Claims 1-6, 9-10 are rejected under 35 U.S.C. & 102(e) as being anticipated by Lumelsky et al, (US 2004/0121460).

Lumelsky teaches a method for inducing differentiation of mouse embryonic stem (ES) cells into insulin producing cells which comprises the steps of: (A) culturing the mouse embryonic stem cells on tissue culture plates, or plates which include a feeder cell layer such as a fibroblast feeder cell layer (e.g. mouse embryonic cell line (STO-1) or primary mouse embryonic fibroblasts treated with UV or anti-proliferative drug such as mitomycin C) in the presence of LIF [paragraph 0091]; (B) generation of embryoid bodies in suspension, thus in the absence of feeder cells [0093], in proliferation medium [0095], in the presence of LIF (1,400 U/ml) [0017]; (C) culturing the EBs in selection-expansion medium (p 9, column 1-2); (D)

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differentiation of the expanded pancreatic endocrine cell stem cells into insulin secreting cells [0114, 0114, 0118].

Lumelsky teaches 1,400 U/ml or 1000 U/ml of LIF in the medium of step B [0017]; 5-30 ng/ml bFGF [0108]; nicotinamide, insulin and fibronectin in the serum-free culture medium, wherein the insulin producing cells are islet-like clusters (see figure 1, stage 5). **Lumelsky** also teaches the differentiation medium of step D comprises nicotinamide [0114] and the medium is similar to culture medium which contains laminin ([0098, lines 7] and insulin [0099]. **Lumelsky** teaches the insulin producing cells induced from mouse ES cells by the method of claim 1 as described above by the A-D steps and the insulin secreting cell clusters induced from mouse ES cells by the method of claim 5 as described in figure 1).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias, Ph.D.
Art Unit 1632

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